

DOCKET NO.: ISIS0170-100 (ISPH-0524)

PATENT

AMENDMENT TO THE CLAIMS: This listing of claims replaces all prior versions and listings of claims in the instant patent application. Claims 34, 36, 51, 59 and 63 are amended and claims 50 and 52 are canceled herein.

Listing of claims:

1-33 (Canceled)

34. (Currently amended) A method of modulation of processing of a selected wild-type cellular mRNA target, said method comprising binding to said wild-type cellular mRNA target in vitro an antisense compound having at least one 2'-guanidinium, 2'-carbamate, or 2'-aminoxy, or 3'-methylene-phosphonate; wherein said antisense compound is specifically hybridizable with said mRNA target and does not elicit cleavage of the mRNA target upon binding, so that processing of said mRNA target is modulated.

35. (Previously presented) The method of claim 34 wherein said modulation of the processing of a selected wild-type cellular mRNA target is modulation of splicing of said mRNA target.

36. (Currently amended) The method of claim 34 wherein said antisense compound has a 2'-guanidinium, 2'-acetamide, 2'-carbamate, or 2'-aminoxy, or 2'-dimethylaminooethoxyethoxy- modification on substantially every sugar.

37. (Previously presented) The method of claim 36 wherein said antisense compound has at least one phosphorothioate backbone linkage.

38. (Previously presented) The method of claim 34 wherein said antisense compound is an antisense oligonucleotide.

39. (Previously presented) The method of claim 35 wherein said modulation of splicing is a redirection of splicing.

40. (Previously presented) The method of claim 35 wherein said modulation of splicing results in an altered ratio of splice products.

41. (Previously presented) The method of claim 35 wherein said modulation of splicing results in exclusion of one or more exons from a mature mRNA.

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42. (Previously presented) The method of claim 41 wherein said antisense compound is targeted to at least a portion of an exon to be excluded.

43. (Previously presented) The method of claim 42 wherein said antisense compound is targeted to an intron-exon junction.

44. (Previously presented) The method of claim 39 wherein said antisense compound is targeted to at least a portion of a region up to 50 nucleobases upstream from a 5' splice site.

45. (Previously presented) The method of claim 44 wherein said redirection of splicing is a decreased frequency of use of said 5' splice site.

46. (Previously presented) The method of claim 34 wherein said processing of a selected wild-type cellular mRNA target is polyadenylation of said mRNA target.

47. (Previously presented) The method of claim 34 wherein said antisense compound is targeted to a polyadenylation signal or polyadenylation site.

48. (Previously presented) The method of claim 34 wherein said processing of a selected wild-type cellular mRNA target is regulating stability of said mRNA target, by targeting said antisense compound to a sequence which controls the stability of said mRNA target.

49. (Previously presented) The method of claim 34 wherein said antisense compound which does not elicit cleavage of the mRNA target upon binding contains at least one modification which increases binding affinity for the mRNA target and which increases nuclease resistance of the antisense compound.

50. (Canceled)

51. (Currently amended) The method of claim 50 claim 34 wherein every nucleoside of said antisense compound has a 2'-guanidinium, 2'-carbamate, or 2'-aminoxy modification of its sugar moiety.

52. (Canceled)

53. (Previously presented) The method of claim 34 wherein said antisense compound which does not elicit cleavage of the mRNA target upon binding contains

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at least one modified backbone linkage other than a phosphorothioate backbone linkage.

54. (Previously presented) The method of claim 53 wherein said antisense compound also contains at least one phosphodiester or phosphorothioate backbone linkage.

55. (Previously presented) The method of claim 53 wherein said modified backbone linkages alternate with phosphodiester and/or phosphorothioate backbone linkages.

56. (Previously presented) The method of claim 53 wherein every backbone linkage is a modified backbone linkage other than a phosphorothioate linkage.

57. (Previously presented) The method of claim 53 wherein said modified backbone linkage is a 3'-methyl phosphonate.

58. (Previously presented) The method of claim 34 wherein said antisense compound which does not elicit cleavage of the mRNA target upon binding contains at least one modified nucleobase.

59. (Currently amended) The method of ~~claim 57~~ claim 58 wherein said modified nucleobase is a C-5 propyne.

60. (Previously presented) The method of claim 40 wherein said altered ratio of splice products results from an increase or a decrease in the amount of a splice product encoding a membrane form of a protein relative to a soluble form of a protein.

61. (Previously presented) The method of claim 60 wherein said protein is a receptor.

62. (Previously presented) The method of claim 61 wherein said receptor is a hormone or cytokine receptor.

63. (Currently amended) The method of claim 34 wherein said antisense compound has a 3'-methyl phosphonate at substantially every backbone linkage.